IN THE DRAWINGS:

Please replace Figures 10C-10D with the attached replacement drawing sheet.

REMARKS

In the Office Action dated August 19, 2008, 2008, Claims 1-20 are pending and under consideration. Claims 13, 15 and 19 are objected to for certain informalities. Claims 7, 10, and 14 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claims 12 and 14 are rejected under 35 U.S.C. §112, second paragraph, as allegedly incomplete for omitting essential elements. Claims 2, 5, and 12-19 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Claims 1-9 and 11-20 are rejected under 35 U.S.C. §112, first paragraph for allegedly lacking enhancement. Claims 1-10, 12, 14-18, and 20 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent 5,316,920, as evidenced by U.S. Patent 5,766,570. Claims 1-20 are rejected under 35 U.S.C. 103(a) as allegedly obvious over U.S. Patent 5,316,920, in view of Klansinsirkul et al. (Blood 99: 2586, 2002), as evidenced by U.S. Patent 5,766,570. Claims 1-9 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as allegedly unpatentable over claims 1-8, 11-13, 15-16 and 18-23 of co-pending application 10/523,756, in view of U.S. Patent 5,316,920. The drawings are also objected to.

This Response addresses each of the Examiner's rejections and objections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Drawings

The Examiner objects to the drawings because the Y axis label for Figure 10C is allegedly missing.

Applicants submit that Page 9 of the specification describes Figures 10A-10D and states that Figure 10C is a control relative to A, B and D. Therefore, the Y axis of Figure 10C should read: "% Specific ^{51}-CR Release", as used in Figures 10A, B and D. Accordingly,

Applicants provide herewith a replacement drawing sheet (containing both Figure 10C and 10D) which has included the lablel, "% Specific ^{51}-CR Release", for the Y axis of Figure 10C. Withdrawal of the objection to the drawings is respectfully requested.

Objections to Claims

Claims 13, 15 and 19 are objected to for certain informalities.

In response, claim 13 has been amended to delete the reference to claim 17, and to depend from claim 12 instead. Claim 15 has been amended to delete the term "the" before the term "said". Claim 19 has been amended to replace the term "allergenic" with the term "allogeneic", as supported by the specification, for example, at page 30, line 22.

Therefore, withdrawal of the objections to claims 13, 15 and 19 is therefore respectfully requested.

35 U.S.C. §112, Second Paragraph Rejections

Claims 7, 10, and 14 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

Regarding claim 7, the Examiner has objected to the phrase "the APC and/or lymphocyte" in line 2 as lacking antecedent basis. Claim 7 has been amended to refer to "said cell" instead.

Regarding claim 10, the Examiner notes that this claim refers to "said subject" which is not introduced earlier in the claim. In response, claim 10 has been amended to recite "in a subject" in the preamble.

Regarding claim 14, the Examiner states that the phrase "the lymphocyte" has no antecedent basis. Claim 14 has been amended to read "T cell" instead.

Claims 12 and 14 are also rejected under 35 U.S.C. §112, second paragraph, as allegedly incomplete for omitting essential elements. It is believed that the Examiner meant to reject claims 12 and 15.

Specifically, the Examiner states that the instant claims are drawn to a method for the therapeutic treatment of a condition characterized by the aberrant, unwanted, or otherwise inappropriate immuno-activity of graft. However, the only recited step is contacting the graft with an antibody that binds to CD83. The Examiner alleges that it is unclear how the method results in a treatment of a condition when the claims do not recite that the graft is contacted with the antibody in a subject (i.e., that the antibody is administered to a subject), nor do the claims recite that an antibody-contacted graft is administered to a subject.

Applicants respectfully submit that the specification teaches that the graft can be contacted with an effective agent *in vitro* or *in vivo*. See page 26, lines 4-19 of the specification, for example. One skilled in the art would readily know the additional steps required to carry out either an *in vitro* or *in vivo* method. Therefore, it is respectfully submitted that there is no need to add further method steps to the claims. To further define the *in vitro* and *in vivo* aspect of the present methods, Applicants have added new claims 21-22, which are fully supported explicitly and implicitly by the disclosure in the specification, e.g., page 26, lines 4-19.

In view of the foregoing, it is respectfully submitted that the rejections under 35 U.S.C. §112, second paragraph, are overcome. Withdrawal of the rejections is respectfully requested.

35 U.S.C. §112, First Paragraph Rejection (Written Description)

Claims 2, 5, and 12-19 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Examiner alleges

that there is insufficient written description to demonstrate that the applicants were in possession of the claimed genus of "functional equivalents", "derivatives', "homologs", "analogs", "chemical equivalents", or "mimetics" of an antibody which binds to CD83.

In an effort to favorably advance prosecution, Applicants have amended the claims such that the claims no longer recite "functional equivalents", "derivatives', "homologs", "analogs", "chemical equivalents", or "mimetics". As such, the written description rejection under 35 U.S.C. §112, first paragraph, is overcome, and withdrawal thereof is respectfully requested.

35 U.S.C. §112, First Paragraph Rejection (Enablement)

Claims 1-9 and 11-20 are rejected under 35 U.S.C. §112, first paragraph for allegedly lacking enhancement. The Examiner has acknowledged that the specification is enabling for a method of downregulating the immuno-activity of a myeloid dendritic cell, a T cell, or an immuno-competent graft comprising inducing cell lysis with an antibody or antigen-binding fragment thereof that binds to CD83. However, the Examiner contends that the specification does not provide enablement for the full scope of the method as claimed for the following reasons.

First, the Examiner has objected to the phrase "modulating" in claims 1-9 on the basis that the term encompasses both an increase and decrease in the immune-activity of the cell, or the immune response. The Examiner contends that there is support for a decrease, but not an increase. Applicants have amended independent claims 1, 8 and 9, to replace the term "modulating" with "inhibiting or otherwise down-regulating". Support for this amendment can be found in the specification, for example at page 10, lines 27-31.

The Examiner also objects that claim 20 is drawn to a method that might encompass treating a wide range of conditions. Applicants respectfully submit that the skilled person could readily recognize from both the specification and their own knowledge which diseases or conditions fall with the scope of claim 20.

Firstly, the claim is clearly drawn to a condition "characterized by an aberrant, unwanted or otherwise inappropriate immune response". The specification clearly states this (see page 31, for example). The same paragraph of the specification goes on to provide specific examples of such conditions, including auto-immune conditions, chronic inflammatory conditions, allergies and transplant rejection, as well as conditions generally where undesirable responses are triggered by the presentation of antigen. Specific examples of auto-immune and anti-inflammatory disorders are given in paragraph 3 of page 31.

The specification also discloses what is encompassed within the term "immune response"; for example, the text from page 11, line 31 to page 12, line 1, discloses cell-mediated and humoral immune responses; page 15, line 26 discloses autoimmune responses; page 23, lines 13 and 18 discloses ADCC and the complement system. Moreover, the specification discusses specific diseases associated with a modulated immune response, such as graft versus host disease, graft rejection, and the diseases listed at page 31, liens 9 to 11 and 15 to 17. In the context of graft rejection, the term "immune response" is defined in the last sentence of page 25, paragraph 4 to comprise immune-activity which directly or indirectly contributes to transplant and/or host tissue rejection.

In addition, it is submitted that the skilled person could readily determine other diseases associated with a modulated immune response. For example, the Examiner's attention is drawn to the text book "Samter's Immunologic Diseases" published in 2001, the bibliographic

information for which is attached as **Exhibit 1**. This book provides a comprehensive overview of immunologic diseases and will have formed part of a skilled person's common general knowledge at the priority date, allowing the skilled person to recognize which conditions or diseases fall within the definitions of the presently-filed claims.

The Examiner has also objected to the phrase "preventing" in claims 1-8 and 11-20. The Examiner's objection is raised on the basis that antibody treatment would not result in the lysis of every DC or T cell. The Examiner suggests that the remaining terms "inhibits or otherwise down-regulates" are more appropriate. Applicants have deleted the term "preventing" from the claims.

In view of the foregoing, it is respectfully submitted that those skilled in the art would be able to practice the methods, as presently claimed, without undue experimentation. The enablement rejection under 35 U.S.C. §112, first paragraph, is therefore overcome. Withdrawal of the rejection is respectfully requested.

35 U.S.C. §102(b) Rejection

Claims 1-10, 12, 14-18, and 20 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by U.S. Patent 5,316,920, as evidenced by U.S. Patent 5,766,570.

The '920 patent allegedly teaches that HB15 is a molecule expressed by dendritic cells and Langerhan's cells, as well as activated T cells (see column 5, lines 47-55). As evidenced by the '570 patent, HB15 is another name for CD83 (see column 2, lines 20-23).

It is noted that at column 5, lines 38-39, the '920 patent describes that many T cell lines expressed CD83, "but expression was generally at low levels". The focus of the '920 patent is clearly on CD83 expression in *Langerhans* cells.

Applicants respectfully submit that the '920 patent is speculative at best of the function of CD83 (see for example column 5, line 24 to column 6, line 2). The patent notes a connection between CD83 and cell proliferation based on differential expression in non-activated and activated cells, and states that CD83 is thus "important for maximal growth of lymphoblastoid cells or the maximum growth of cells is critical for expression of this antigen". This indicates that while a connection between cell proliferation and CD83 was made, the inventors of the '920 patent were not able to establish whether modulation of CD83 impacts or has an effect on this part of the cell cycle. It is noted that the '920 patent states at column 14, lines 16-24 that anti-CD83 antibodies partially inhibit proliferation of T cells. However, there does not appear to be any discussion of cell death or lysis anywhere in the '920 patent. Inhibiting cell proliferation is quite different to increasing cell lysis as achieved by the present invention.

Based on expression levels in various tissues, and homology to other members of the Ig superfamily, the '920 patent speculates that CD83 is a lymphocyte cell surface antigen. The '920 patent discloses the production of monoclonal antibodies that are reactive with CD83 (see Example II at column 8, lines 34-58).

Applicants respectfully submit that only after function has been established, potential applications can be proposed. Given that the '920 patent is speculative of the function of CD83, the potential applications of CD83 or anti-CD83 antibodies are even more tentative. In this regard, the portion of this '920 patent that has any possible relevance to the claimed invention is the discussion under the heading "Use" in columns 13 to 14, including the following statement at lines 19-29:

> "...since Langerhans cells are the primary immunocompetent cell in the skin, playing a role in the presentation of antigen to T cells and the induction of contact hypersensitivity, and **since [CD83] is expressed by Langerhans cells** and may be involved in antigen presentation, it is **likely** to be involved in the

> pathogenesis of human skin disease such as psoriasis, autoimmune disorders, organ transplants an AIDS. ... Therefore, antagonists to [CD83] function can provide important therapeutic agents for treatment of these diseases."

This is clearly a postulated application, not supported by any example, and based on the high levels of expression CD83 discovered in *Langerhans cells*.

The Examiner, however, states that "the method" of the '920 patent would inherently result in the contact of DCs or T cells with the anti-CD83 antibody *in vivo*, and would also inherently result in the lysis of said cells.

Applicants respectfully disagree. The '920 patent does not provide clear and adequate teaching for any method based on either administration of an anti-CD83 antibody to a subject, or contacting a graft with an anti-CD83 antibody *in vitro* prior to transplantation, as claimed in the present application. There is only speculation as to potential applications of CD-83 or its antibodies. For a claim to lack novelty, the prior art must teach each essential feature of the claim. The '920 patent does not disclose a contacting step of the claimed method wherein the graft is contacted (either *in vitro* or *in vivo*) with an antibody or antigen-binding fragment thereof (see claims 12, 15 and 21-22), or an administration step wherein the antibody or antigen-binding fragment thereof is administered to the subject (see claim 20). Therefore, Applicants respectfully submit that the '920 patent fails to teach each and every element of the claimed invention.

Accordingly, the rejection under 35 U.S.C. §102(b) based on the '920 patent is overcome. Withdrawal of the rejection is respectfully requested.

35 U.S.C. §103(a) Rejection

Claims 1-20 are rejected under 35 U.S.C. 103(a) as allegedly obvious over U.S. Patent 5,316,920, in view of Klansinsirkul et al. (Blood 99: 2586, 2002), as evidenced by U.S. Patent 5,766,570.

The Examiner states that although the '920 patent does not disclose allogeneic bone marrow transplantation, it would be obvious to combine this patent with Klansansirkul, which teaches that antibodies to T cells and dendritic cells are useful for administration to recipients of bone marrow transplantation. Klansansirkul discloses an anti-CD52 antibody and demonstrates that this antibody killed purified DCs *in vitro* and depleted DCs *in vivo*.

Applicants respectfully submit that no cell lysis or depletion by an anti-CD83 antibody is taught by Klansansirkul or the '920 patent. Applicants further respectfully submit that the two citations are sufficiently removed from each other that those skilled in the art would not have been motivated to combine the two; and further, even if a motivation had existed, there would have been no reasonable expectation of success in arrived at the claimed invention, especially considering the unpredictability in the art.

Accordingly, it is respectfully submitted that the presently claimed invention is unobvious in view of the cited references in combination. Withdrawal of the rejection under 35 U.S.C. 103(a) based on the '920 patent and Klansinsirkul is respectfully requested.

Non-Statutory Double Patenting

Claims 1-9 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as allegedly unpatentable over claims 1-8, 11-13, 15-16 and 18-23 of co-pending application 10/523,756, in view of U.S. Patent 5,316,920.

Applicants acknowledge that the rejection is provisional, and therefore will address the rejection once the claims are deemed otherwise allowable.

Conclusion

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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EXHIBIT 1

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Samter's Immunologic Diseases

Source: Lippincott Williams & Wilkins (LWW)

Author(s): Frank Austen MD; Michael M. Frank MD; John P. Atkinson MD; Harvey I. Cantor MD

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